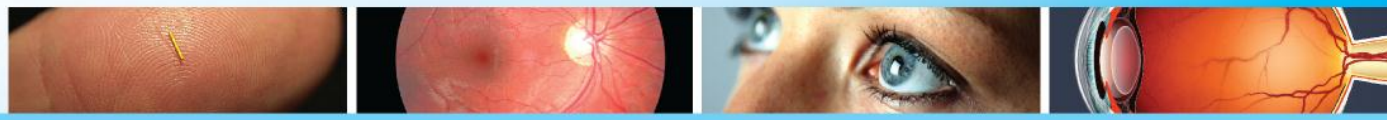
pSivida Corp

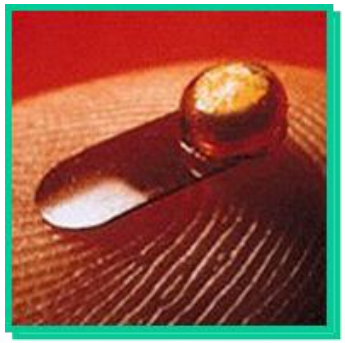
10th Annual NanoBusiness Conference, Boston
NanoMedicine Panel, Monday Sept 26, 2011



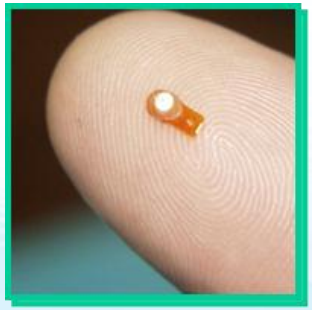
DRUG DELIVERY and NANOSTRUCTURING: DIVERGENT EFFECTS

Hong Guo, PhD
Vice President of Research
pSivida Inc.

Evolution of pSivida's Drug Delivery Systems

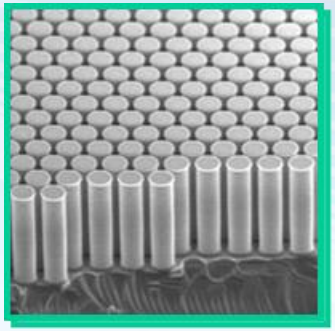


1st Generation



2nd Generation

3rd Generation



4th Generation

ILUVIEN for Diabetic Macular Edema (Alimera Sciences)

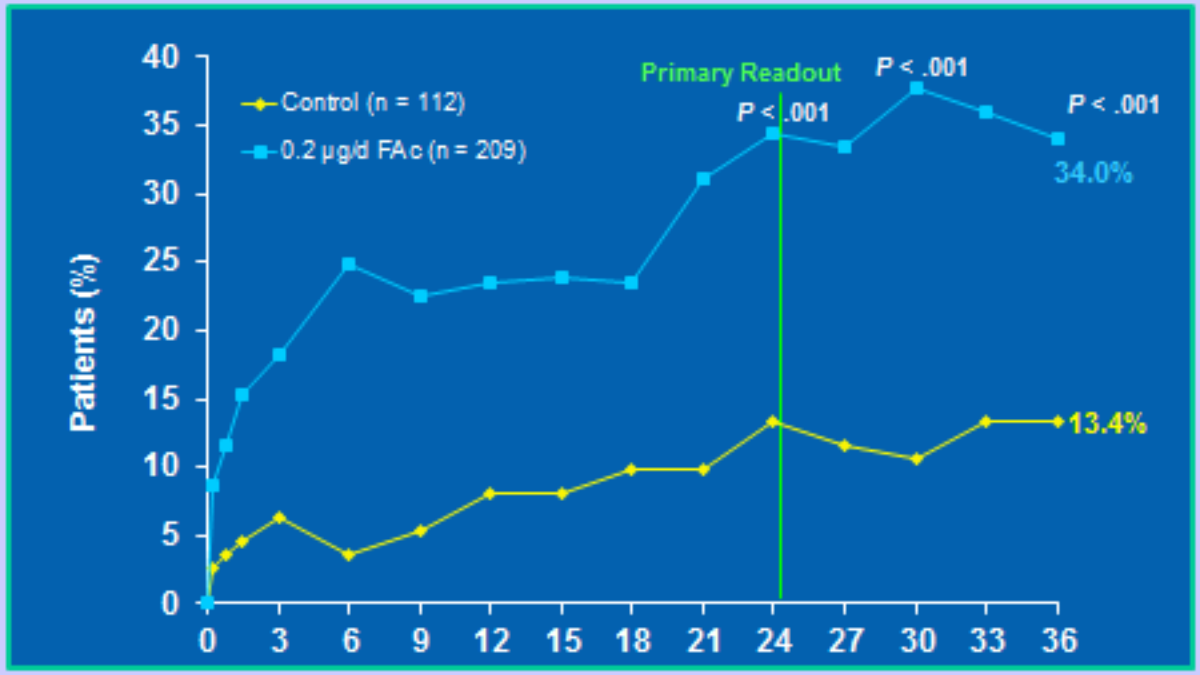
DME

- Affects 1m in US
- Leading cause of vision loss in people under 65
- Laser therapy (burns to retina) limited efficacy
- No FDA approved drug treatments
- US Market estimated $1.5-4B

Iluvien Status

- Phase III clinical trials in approx. 1,000 patients
- NDA given Priority Review
- Received CRL December 2010
- Positive 36 month data released in Feb, subgroup analysis in May
- Resubmitted May 2011
- Potential approval in Q4 2011

Efficacy in Patients with Chronic DME



ILUVIEN Side Effects

Intraocular Pressure (IOP) > 30mm Hg
3 Years All Patients: 14.1% risk
18.4 % Iluvien vs 4.3% control
4.8% required procedure
3 Years Chronic DME: 9.4% risk
14.8% Iluvien vs 5.4% control
5.2% required procedure

Cataract
34% of patients in trial had already undergone cataract surgery
Approx. 85% of low dose patients developed cataract

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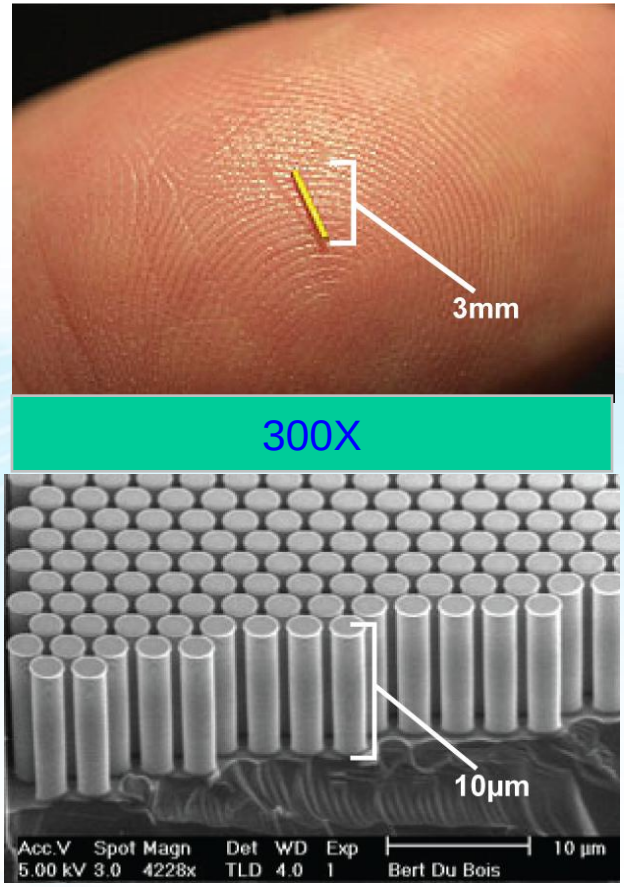
New Generation Drug Delivery Technologies



- Fully bio-erodible
- Potential to deliver drugs, peptides and proteins
- Very promising preliminary data

BioSilicon: A highly porous material

1cm3 of bioSilicon™
i.e. sugar cube

Total surface area
equivalent
to 2 tennis courts

If the columnar pores were
Stacked the length would
measure 6 million miles

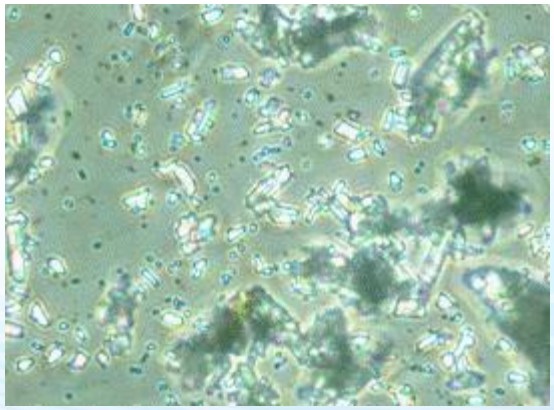
BioSilicon Technology

BioSilicon Technology:
Stabilization of amorphous forms
Enhanced dissolution and Bioavailability of poorly soluble molecules

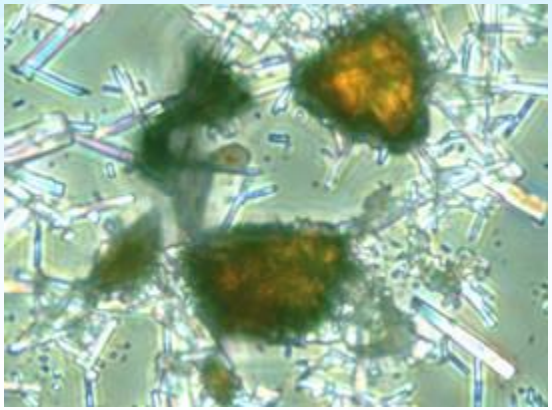
Tethadur Systems:
Protein Adsorption
Sustained Release Anti-Bodies

Drug Loaded BioSilicon

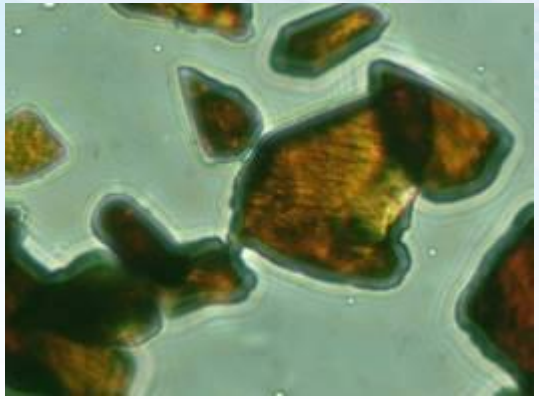
BioSilicon



Unprocessed API



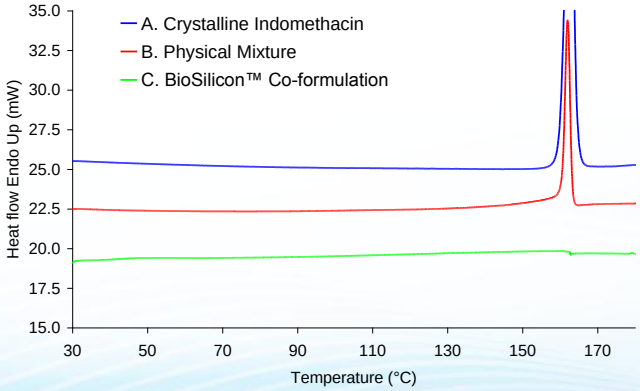
API and BioSilicon



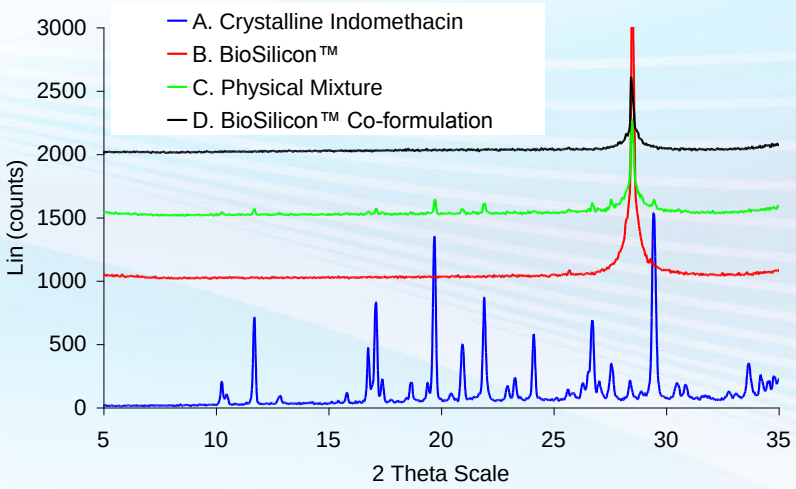
API in BioSilicon

Indomethacin in BioSilicon

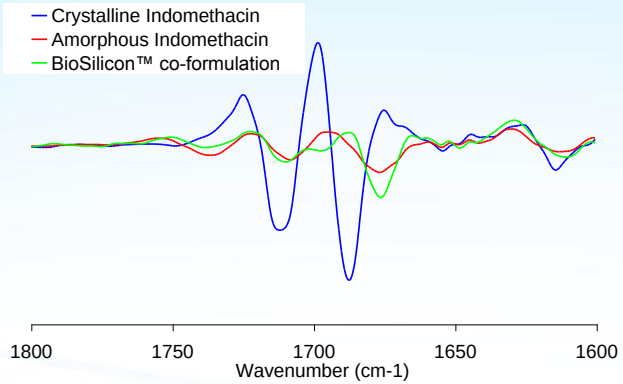
DSC Analysis



XRD Analysis

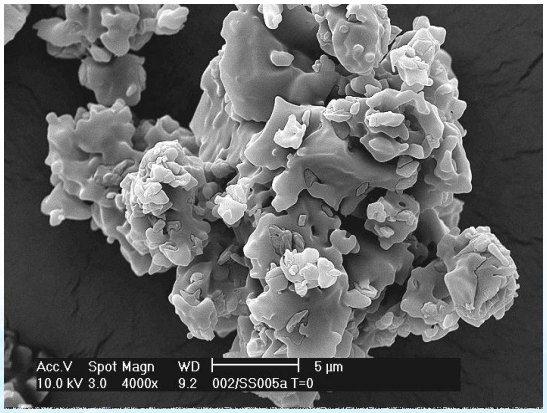


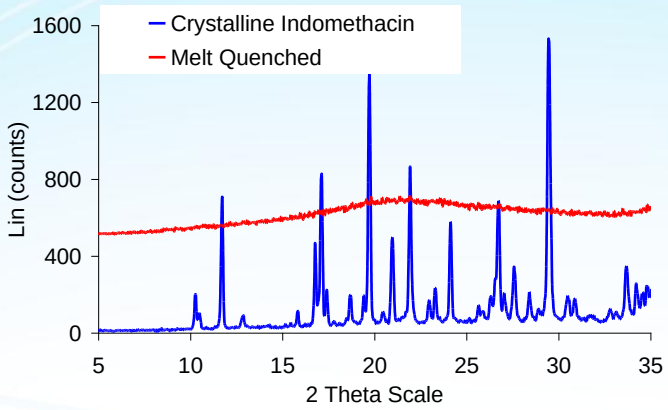
FTRI Analysis



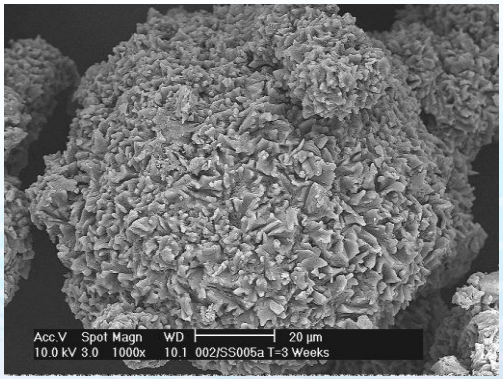
Stability of Amorphous Indomethacin

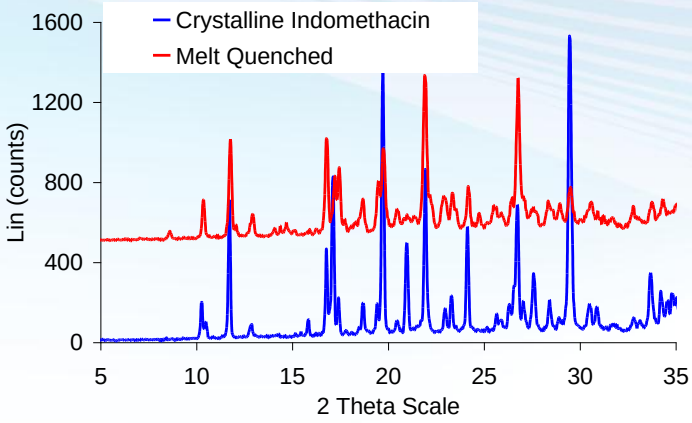
Time 0





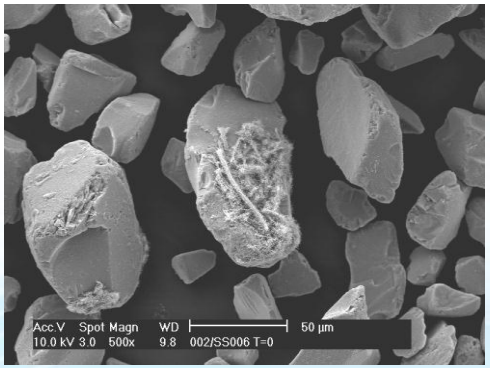
Weeks at 40°C/ 75% RH

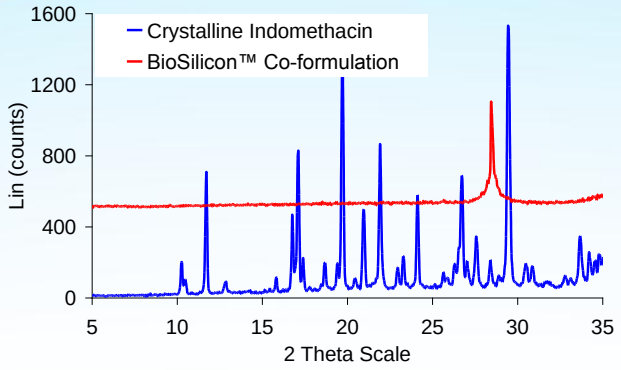




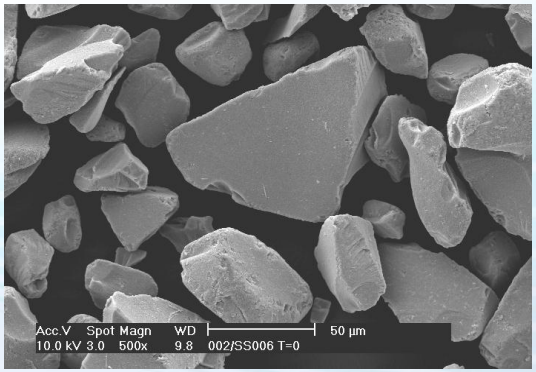
Indomethacin in BioSilicon

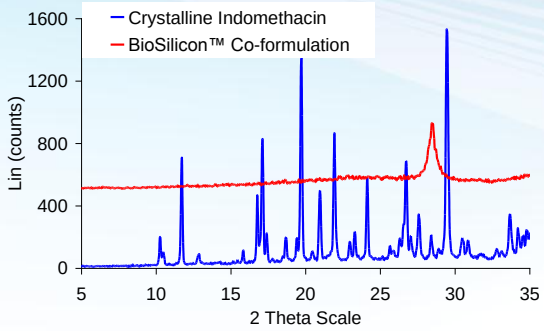
Time 0





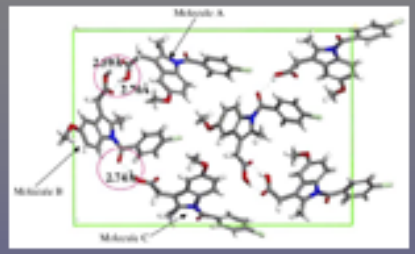
6 month at 40°C/ 75% RH



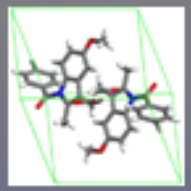


Stabilization of Amorophous Form

a=5.4Å
b=25.3Å
c=18.52Å

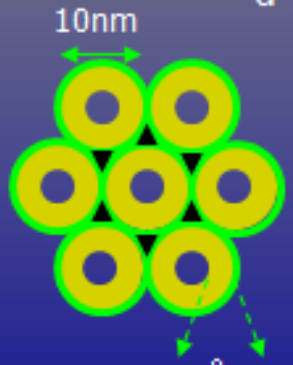


α-polymorph



a=9.3Å
b=11.0Å
c=9.7Å

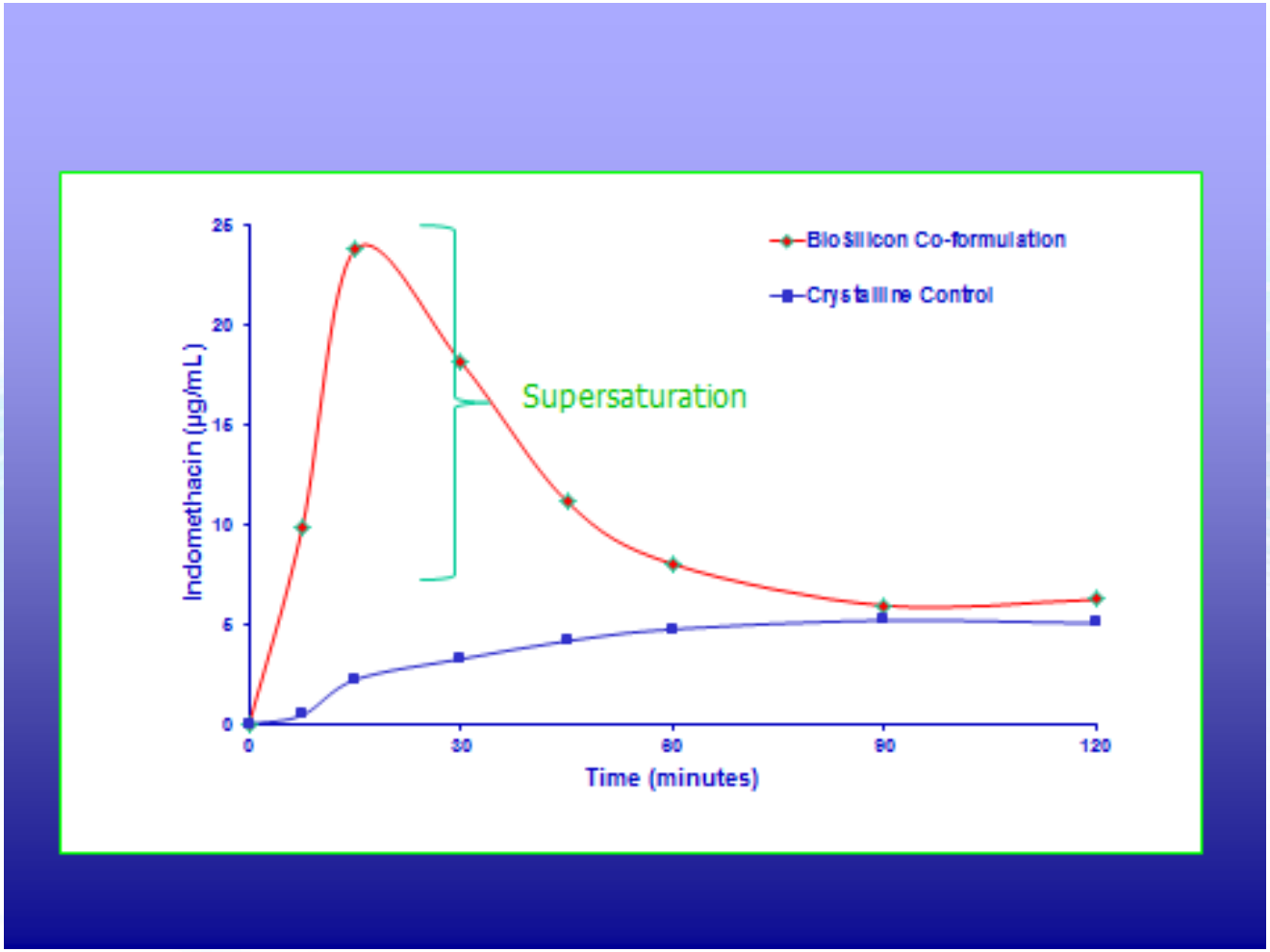
γ-polymorph



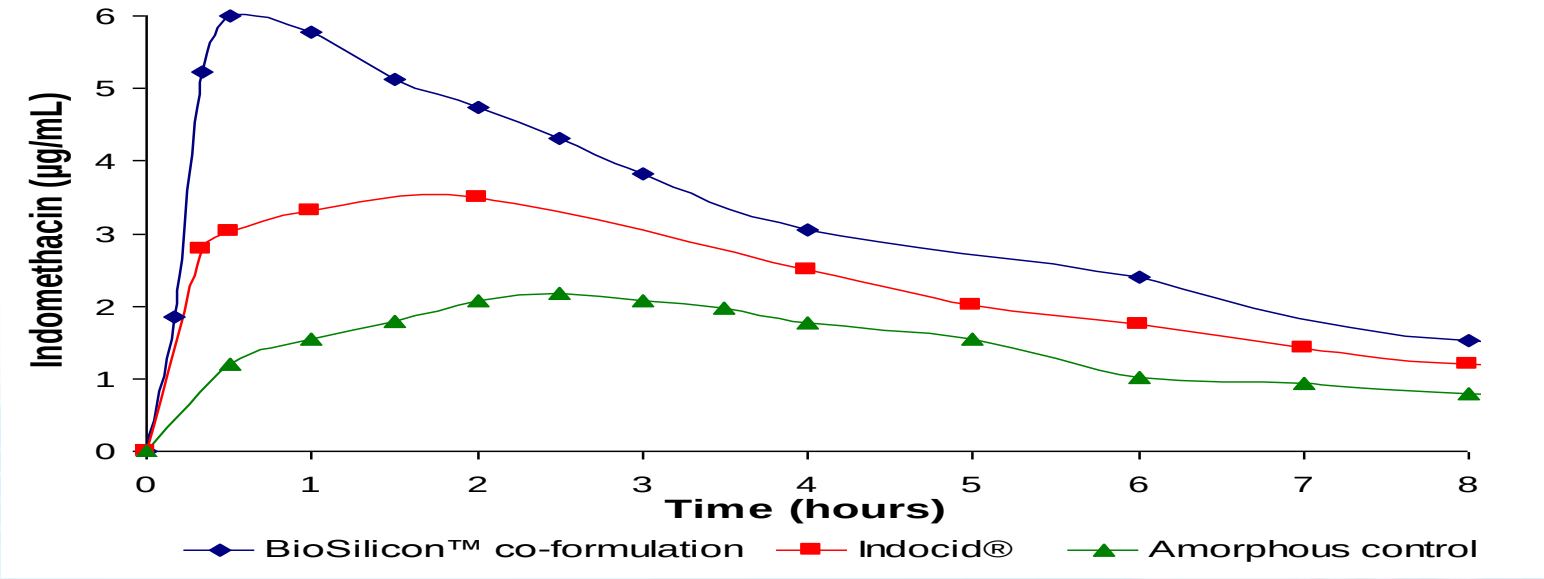
- 20% (w/w) drug loading
- Drug molecule = 4.8Å at longest dimension
- Drug layer = 22Å
- Drug layer is 4 molecules thick
- Insufficient volume to allow recrystallisation

- **Physically stabilised amorphous form**

Indomethacin Dissolution



Indomethacin Oral Bioavailability



Pharmacokinetic Parameter		Indomethacin I.V.	Control	BioSilicon Co-formulation	Indocid®
T_{max}	(h)	n/a	2.75 ± 0.65	0.56 ± 0.31	2.00 ± 0.00
C_{max}	(µg/ml)	n/a	2.48 ± 0.38	6.46 ± 0.52	3.49 ± 0.54
$AUC_{0\text{-}24h}$	(h*µg/ml/mg)	66.92 ± 6.73	35.83 ± 1.95	66.98 ± 2.62	51.82 ± 2.33
F (%)	(n/a)	n/a	53.54 ± 2.91	100.1 ± 3.9	77.43 ± 3.49

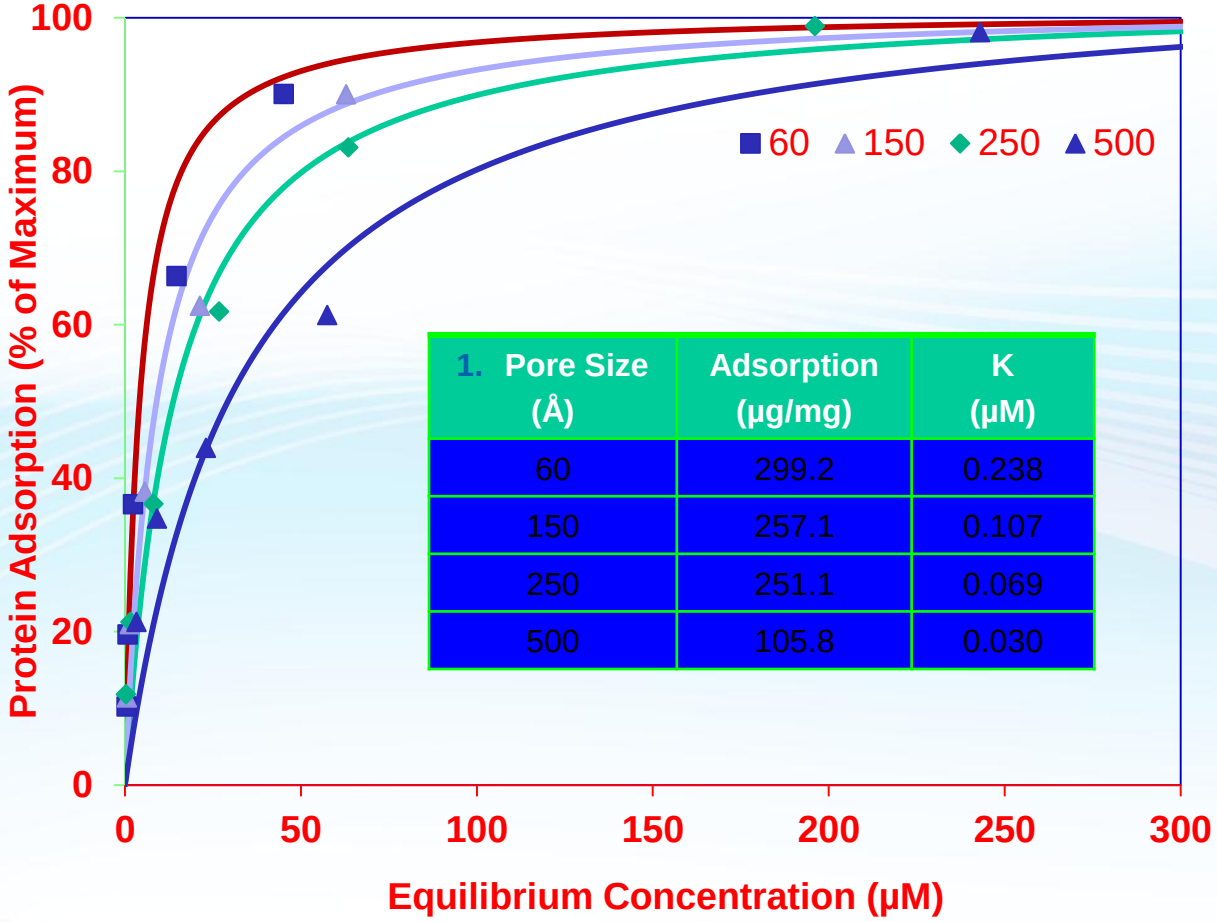
Sprague-Dawley rates (n=3)

Tethadur Technology
Sustained Release of Proteins

Tethadur System

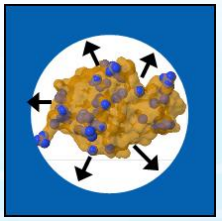
- Fully bioerodible
- Microparticulate (< 10 µm)
- Nanostructured
- Can be tailored to adsorb and release proteins

Protein Adsorption

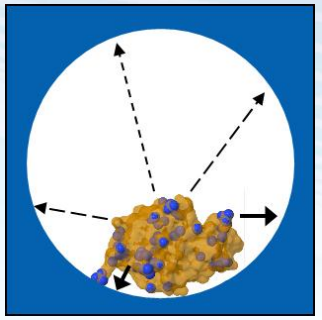


1. Pore Size (Å)	Adsorption (µg/mg)	K (µM)
60	299.2	0.238
150	257.1	0.107
250	251.1	0.069
500	105.8	0.030

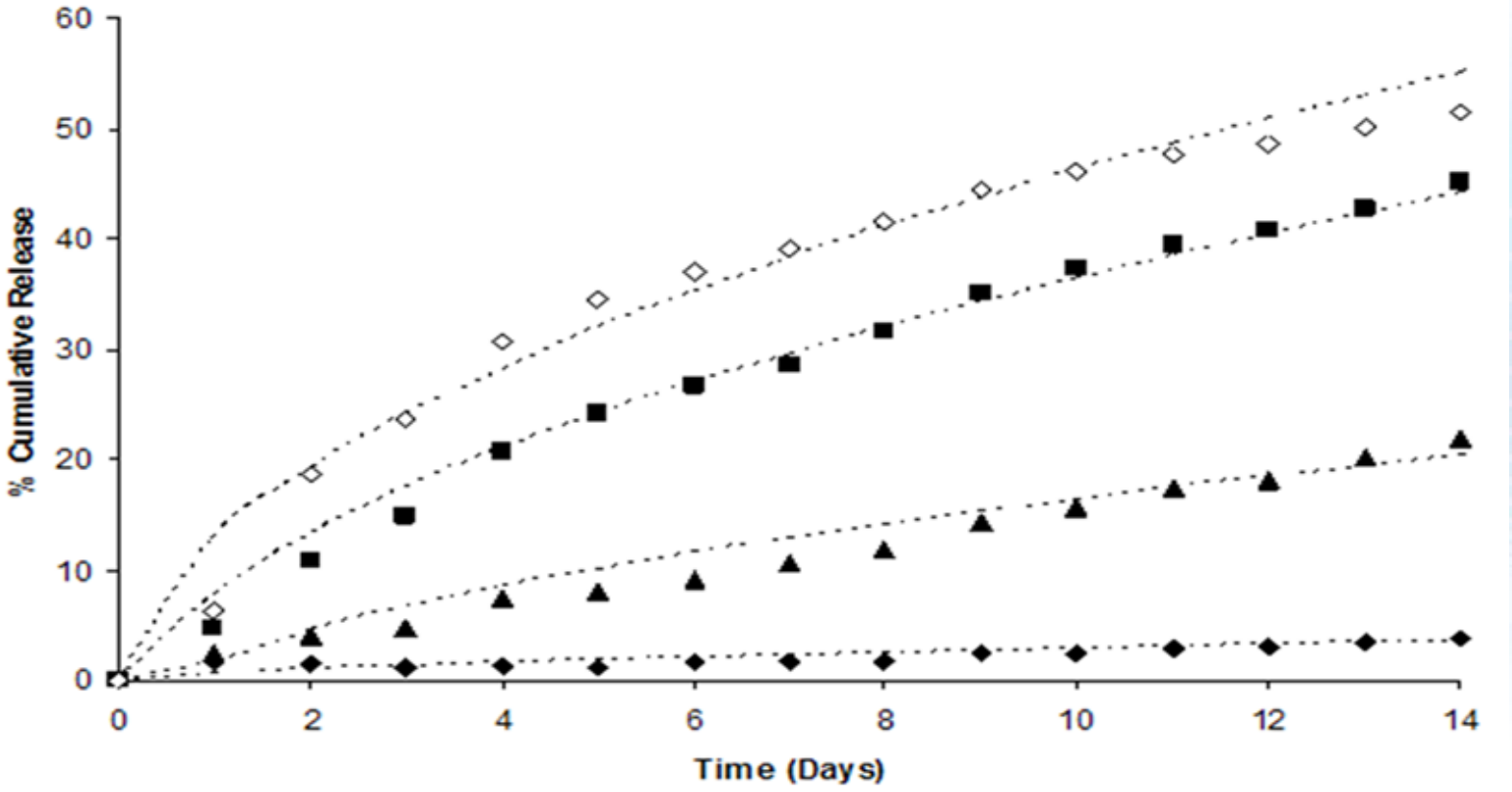
60Å



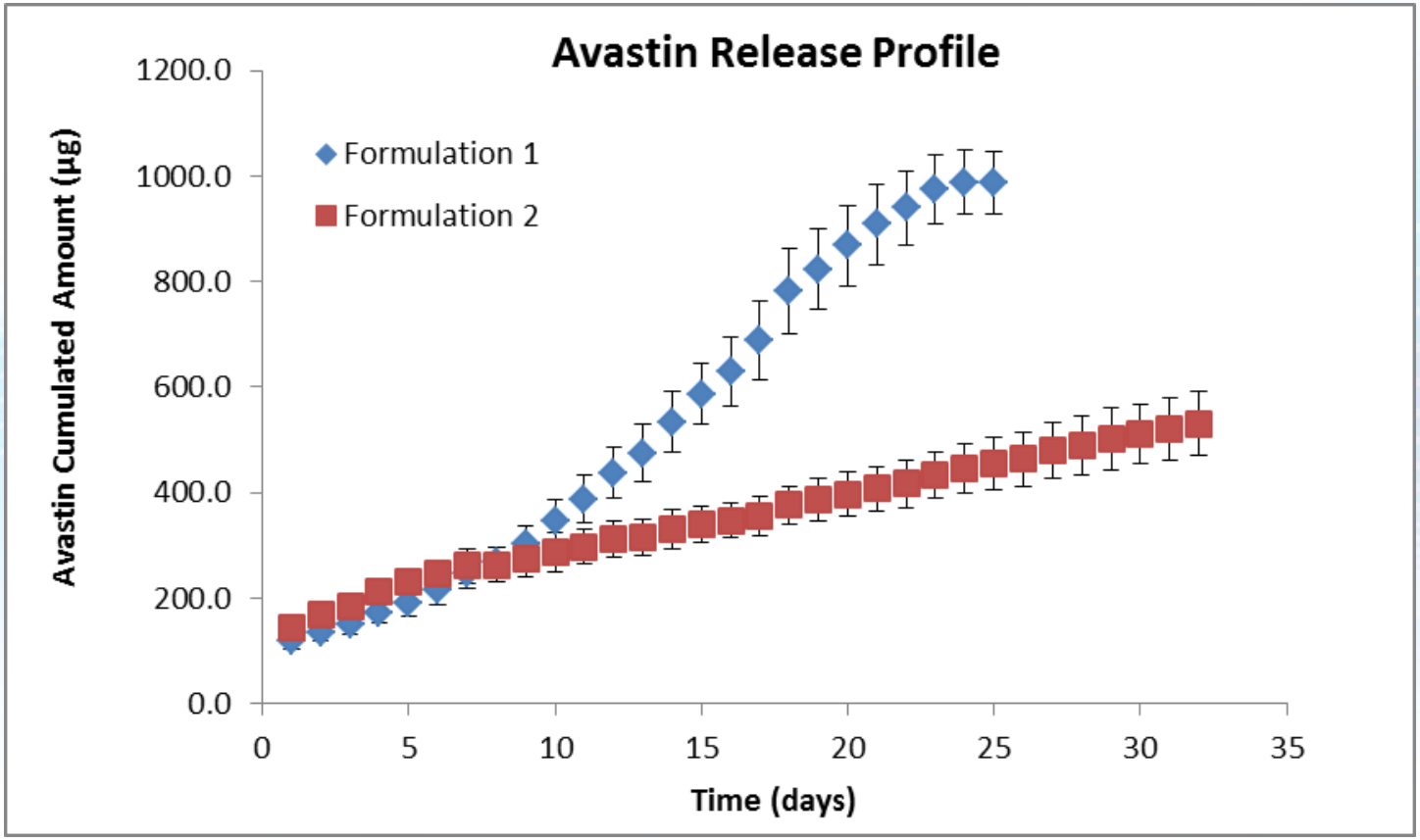
250Å



Effect of Pore Size on Protein Release Rate



In-Vitro Release Rate of “real” Protein



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SUMMARY

- Nano-structuring can maintain target molecules in amorphous form
- Effect on release a function of elimination of lattice energy versus creation of agent/wall interaction
- Agent/wall interaction adjustable allowing release rate to be controlled